Patent

carbon atoms, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, carboxyalkyl of 2-7 carbon atoms, carboalkoxyalky of 3-8 carbon atoms, aminoalkyl of 1-5 carbon atoms, N-alkylaminoalkyl of 2-9 carbon atoms, N,N-dialkylaminoalkyl of 3-10 carbon atoms, N-alkylaminoalkoxy of 2-9 carbon atoms, N,N-dialkylaminoalkoxy of 3-10 carbon atoms, mercapto, methylmercapto, and benzoylamino;

Z is NH-, O-, S-, or NR-;

R is alkyl of 1-6 carbon atoms, or carboalkyl of 2-7 carbon atoms;

G<sub>1</sub>, G<sub>2</sub>, R<sub>1</sub>, and R<sub>4</sub>-are each, independently, hydrogen, halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, alkenyloxy of 2-6 carbon atoms, hydroxymethyl, halomethyl, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, alkynoyloxymethyl of 4-9 carbon atoms, alkynoyloxymethyl of 4-9 carbon atoms, alkynoyloxymethyl of 4-9 carbon atoms, alkoxymethyl of 2-7 carbon atoms, alkylsulphinyl of 1-6 carbon atoms, alkylsulphinyl of 1-6 carbon atoms, alkylsulphinyl of 1-6 carbon atoms, alkylsulfonamido of 1-6 carbon atoms, alkynylsulfonamido of 2-6 carbon atoms, hydroxy, trifluoromethyl, trifluoromethoxy, cyano, nitro, carboxy, carboalkoxy of 2-7 carbon atoms, carboalkyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzyl, amino, hydroxyamino, alkoxyamino of 1-4 carbon atoms, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, N alkylamino of 1-6 carbon atoms, N-alkyl-N-alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms, phenylamino, benzylamino,

$$R_7$$
- $(C(R_6)_2)_p$   $N$ - $(C(R_6)_2)_k$ -Y-  $R_8$   $R_9$ -CH-M- $(C(R_6)_2)_k$ -Y-  $(C(R_6)_2)_p$ 

 $R_7$ - $(C(R_6)_2)_g$ -Y- ,  $R_7$ - $(C(R_6)_2)_p$ -M- $(C(R_6)_2)_k$ -Y- , or Het- $(C(R_6)_2)_q$ -W- $(C(R_6)_2)_k$ -Y- with the proviso that either  $G_1$ - or  $G_2$ - or both  $G_1$ - and  $G_2$ - must be a radical selected from the group



Patent

$$R'_{7}-(C(R_{6})_{2})_{g}-Y-R_{7}-(C(R_{6})_{2})_{p}-M-(C(R_{6})_{2})_{k}-Y-Het-(C(R_{6})_{2})_{d}-W-(C(R_{6})_{2})_{k}-Y-R_{7}-(C(R_{6})_{2})_{d}-W-(C(R_$$

Y is a divalent radical selected from the group consisting of

$$-(CH_2)_a$$
,  $-O$ , and  $-N$ ,  $R_6$ 

 $R_7$  is  $-NR_6R_6$ , -J,  $-OR_6$ ,  $-N(R_6)_3$ -+ or  $-NR_6(OR_6)_7$ 

R'7-is—NR<sub>6</sub>(OR<sub>6</sub>), N(R<sub>6</sub>)<sub>3</sub>-<sup>†</sup>, alkenoxy of 1-6 carbon atoms, alkynoxy of 1-6 carbon atoms, N-alkyl-N-alkenylamino of 4-to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms, N-alkyl-N-alkynylamino of 4-to 12 carbon atoms, N-alkenyl-N-alkynylamino of 4-to 12 carbon atoms with the proviso that the alkenyl or alkynyl moiety is bound to a nitrogen or oxygen atom through a saturated carbon atom;

$$M ext{ is } > NR_6, -O_-, > N_-(C(R_6)_2)_p NR_6R_6, \text{ or } > N_-(C(R_6)_2)_p -OR_6;$$

W is  $> NR_6$ , O or is a bond;

Het is a heterocycle selected from the group consisting of morpholine, thiomorpholine, thiomorpholine S-oxide, thiomorpholine S,S-dioxide, piperidine, pyrrolidine, aziridine, pyridine, imidazole, 1,2,3-triazole, 1,2,4-triazole, thiazole, thiazolidine, tetrazole, piperazine, furan, thiophene, tetrahydrothiophene, tetrahydrofuran, dioxane,

1,3-dioxolane, tetrahydropyran, and

wherein the heterocycle is optionally mono- or di-substituted on carbon or nitrogen with  $R_6$ , optionally mono- or di-substituted on carbon with hydroxy,  $-N(R_6)_{2,-}$  or -  $OR_6$ , optionally mono- or di-substituted on carbon with the mono-valent radicals

Patent

 $(C(R_6)_2)_sOR_6$  or  $(C(R_6)_2)_sN(R_6)_2$ , or optionally mono or di-substituted on a saturated carbon with divalent radicals -O or  $-O(C(R_6)_2)_sO$ ;

R6 is hydrogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 1-6 carbon atoms, carboalkyl of 2-7 carbon atoms, carboxyalkyl (2-7 carbon atoms), phenyl, or phenyl optionally substituted with one or more halogen, alkoxy of 1-6 carbon atoms, trifluoromethyl, amino, alkylamino of 1-3 carbon atoms, dialkylamino of 2-6 carbon atoms, nitro, cyano, azido, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, carboxyl, carboalkoxy of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, or alkyl of 1-6 carbon atoms;

R2, is selected from the group consisting of



Patent

Patent

R<sub>3</sub> is independently hydrogen, alkyl of 1-6 carbon atoms, carboxy, carboalkoxy of 1-6 carbon atoms, phenyl, carboalkyl of 2-7 carbon atoms,

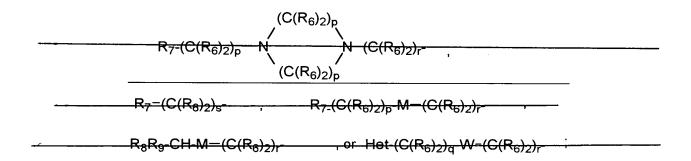
with the proviso that at least one of the R3-groups is selected from the group

$$\frac{(C(R_6)_2)_p}{R_7 \cdot (C(R_6)_2)_p} = N - (C(R_6)_2)_{r^-},$$

$$\frac{(C(R_6)_2)_p}{(C(R_6)_2)_p} = \frac{R'_7 - (C(R_6)_2)_p}{R_8R_9 - CH - M} \cdot \frac{(C(R_6)_2)_r}{(C(R_6)_2)_r} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_6)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_6)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_6)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_6)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_6)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_6)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_6)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_8)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_8)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_8)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_8)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_8)_2)_r}{R_8R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_8R_9 - CH - M} \cdot \frac{(C(R_8)_2)_r}{R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_9 - CH - M} \cdot \frac{(C(R_8)_2)_r}{R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_9 - CH - M} = \frac{R_8R_9 - CH - M}{R_9 - CH - M} \cdot \frac{R_9R_9 - CH - M}{R_9 - CH} = \frac{R_9R_9 - CH}{R_9 -$$

Patent

R5 is independently hydrogen, alkyl of 1-6 carbon atoms, carboxy, carboalkoxy of 1-6 carbon atoms, phenyl, carboalkyl of 2-7 carbon atoms,



Rg, and Rg are each, independently, -(C(R<sub>6</sub>)<sub>2</sub>)<sub>r</sub>NR<sub>6</sub>R<sub>6</sub>, or -(C(R<sub>6</sub>)<sub>2</sub>)<sub>r</sub>OR<sub>6</sub>;

Jis independently hydrogen, chlorine, fluorine, or bromine;

-Q is alkyl of 1-6 carbon atoms or hydrogen;

a = 0 or 1;

g = 1-6;

k = 0.4

n is 0-1;

p = 2-4;

q=0-4;

r = 1.4;

s = 1-6;

u = 0.4 and v = 0.4, wherein the sum of u+v is 2.4;

or a pharmaceutically acceptable salt thereof,

provided that

when R<sub>6</sub> is alkenyl of 2-7 carbon atoms or alkynyl of 2-7 carbon atoms, such alkenyl or alkynyl moiety is bound to a nitrogen or oxygen-atom through a saturated carbon atom;

and further provided that

when Y is -NR6- and R7 is -NR6R6, -N(R6)3-
$$^+$$
, or -NR6(OR6), then  $g = 2-6$ ; when M is -O- and R7-is -OR6, then  $p = 1-4$ ;

